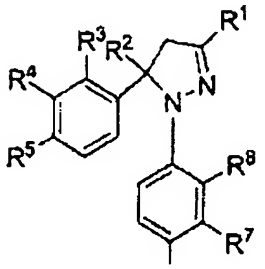
III. REMARKS

Claims 1-12 are currently pending in the application. Claims 10-12 are withdrawn from consideration. Claims 1-9 stand rejected.

Claim Rejections - 35 *USC § 103*

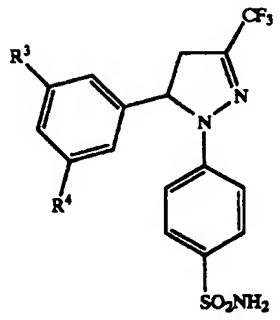
Claims 1-9 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Cuberes-Altisent et al. (WO 99/62884, 1999, US 6,353,117), taken alone.

Cuberes-Altisent et al. describes compounds of the general formula (I), below:

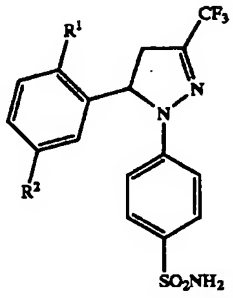


(I)

Applicants' compounds are set forth below:



I



I'

The compounds taught by Cuberes-Altisent et al. are useful for the treatment of inflammation, neoplastic disorders, angiogenesis-mediated disorders and in the treatment of other diseases in which the enzyme cyclooxygenase-2 (COX-2) plays a crucial part.

As recognized by the examiner, the compounds of the prior art are not the same as applicants' compounds. The difference between the prior art of Cuberes-Altisent et al. and the compounds of formula I in the instant application are pointed out in the scheme above, showing the positioning of the methyl substituents on the phenyl ring (all with respect to the heterocyclic substituent).

The difference between the prior art of Cuberes-Altisent et al. and the compounds of formula I' in the instant application is the positioning of the phenyl substituents.

The Examiner is of the opinion that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results.

Applicant respectfully disagrees with the view of the Examiner. The substitution of methyl for hydrogen on a known compound, in particular on an aromatic ring system such as a phenyl ring, cannot be regarded as an obvious modification, even in the absence of any unexpected results.

However, in the present application, not only is there an unobvious substitution in methyl and hydrogen in the compound itself, but in addition, applicant's compounds show an unexpected result.

As to the structural similarity, applicant points out that the substitution of methyl for hydrogen on a known compound, in particular on an aromatic ring system such as a phenyl ring, cannot be regarded as an obvious modification, even in the absence of any unexpected results.

A methyl radical is far more electron rich and also more sterically demanding than a hydrogen radical. In addition, two methyl substituents on a phenyl ring interact and can alter the electronic properties of a phenyl ring substantially by means of the mesomeric and inductive effect. This interaction strongly depends on the substitution pattern of the methyl radicals on the phenyl ring; thus, the electronic properties of the phenyl ring are altered depending on the substitution pattern of the methyl substituents.

The prior art does not describe how a phenyl ring has to be modified in compounds of formula (I) of Cuberes-Altisent et al. to obtain further compounds that are also pharmacologically active. A person skilled in the art would not know if the compounds have to be more electron rich or more electron poor. Thus, it is only with the benefit of hindsight, having seen applicants' disclosure, that one skilled in the art would consider the present claimed compounds. It is both unexpected and surprising that the inventively claimed compounds of formula I and of formula I' are also pharmacologically active.

The examiner states that the motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (i.e. pharmacological use). "Similar activity" as used in the pertinent case law does not mean simply that the two compounds both have some

physiological activity, i.e. pharmacological use. The psychological activity must be the same or at least similar. The 'common properties" recognized by the case law cited by the examiner requires the presence of a same or at worse, similar psychological effect.

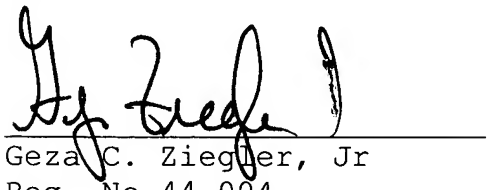
Thus, the compounds of the present invention do demonstrate an unexpected result, because they do not inhibit the enzymes cyclooxygenase-1 and/or cyclooxygenase-2 (see paragraphs 5 and 69 of the present published patent application US 2005/0182119), but do show very good activity in the treatment of cancer as shown in the *in vitro* assays (Table 3).

There is no hint in the prior art that the pyrazoline compounds described therein show any activity in the treatment of cancer. Thus, it is even more unexpected and surprising that the inventively claimed pyrazoline compounds of general formula I and of general formula I' are pharmacologically active and particularly useful in the treatment of cancer.

For all of the foregoing reasons, favorable reconsideration and allowance is respectfully requested. Should any unresolved issues remain, the Examiner is invited to call Applicants' attorney at the telephone number indicated below.

The Commissioner is hereby authorized to charge payment for any fees associated with this communication or credit any over payment to Deposit Account No. 16-1350.

Respectfully submitted,



4/10/2006

Geza C. Ziegler, Jr
Reg. No.44,004

Date

Perman & Green, LLP
425 Post Road
Fairfield, CT 06824
(203) 259-1800
Customer No.: 2512

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service on the date indicated below as first class mail in an envelope addressed to the Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Date: April 10, 2006

Signature: Meaghen Baye
Person Making Deposit